

DESCRIPTION OF THE PROPOSED EXPERIMENT IN NON-TECHNICAL LANGUAGE

Cystic fibrosis (CF) is a common inherited disease among the white population of Europe and North America. It is characterized by chronic infection and obstruction of the airways leading to the lungs. Patients commonly die from the disease by their mid-to-late twenties. The recent discovery and characterization of the inherited material — the gene — that causes the disease has led to a rapid increase in our knowledge of the basic defect responsible for the disease state, and has raised the possibility of treating CF by giving to the patient a good copy of the CF-associated gene. This is a new approach to the treatment of inherited diseases, called gene transfer.

Eventually gene transfer for cystic fibrosis might be achieved by treating the airways of CF patients with a "tailor-made" virus that has been altered to make it less infectious and to include the CF gene. One possible virus to do this is called adenovirus. It is normally associated with minor respiratory infections, such as colds. Although adenoviruses have been used safely in the past as vaccines, we need to establish the feasibility and safety of using such an approach for treatment of cystic fibrosis.

The sponsors of this proposal have already treated eight CF patients with very small amounts of CF-adenovirus and shown it is possible to correct the basic defect associated with the disease. In two studies virus was applied to a small area within the nose and a small electrode used to measure the tiny voltage that normally exists across the lining of the nose. In patients with CF, this voltage is abnormal because of a defect in the CF gene. After administration of virus, this voltage was temporarily restored to normal.

We are extending these studies to ascertain whether it is safe to administer virus to the lung in amounts that are believed to be large enough to correct the defect in the CF gene, and whether virus can be introduced safely into the lung by aerosol treatment — breathing in a mist of virus. The first study, "Adenovirus-Mediated Gene Transfer for Cystic Fibrosis: Safety of Single Administration to the Lung" will evaluate administration of the virus to a small part of the lung (a lobe) by a bronchoscope, a tube commonly used in pulmonary medicine which allows visualization of the airways. If no problems occur after a total of six patients have received two different doses (3 in each dose group), this aerosol study will begin. By testing aerosol administration of the virus the lung, starting with small doses, we can learn if this widely used and noninvasive method of lung treatment can be safely used with our virus vector. In this way, we hope to maximize patient safety, while at the same time determining whether adenovirus is likely to be safe for use in CF patients.